

## Honored Guest's Address

### Beyond *Flatland*

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**M**r President, thank you for your kind introduction. Members of the Association, ladies and gentlemen, I am flattered to be the honored guest of The American Association for Thoracic Surgery. This is a unique opportunity to publicly express my gratitude to the Association for having been awarded the 1973 Evarts Graham Fellowship, which has been a cornerstone in my career.

It is a privilege to pay tribute to my North American mentors. Three of them were presidents of the Association: Frank Gerbode, Dwight McGoon, and Robert Wallace. I should also like to mention Donald Hill from the Pacific Medical Centre in San Francisco and Gordon Danielson from the Mayo Clinic. Finally, I should like to share today's honor with all my colleagues at Great Ormond Street Hospital, London.

The topic chosen for this lecture is an old one that I have, I am afraid, touched upon on several occasions. I will attempt today to show how my thoughts on these matters have evolved, but I must apologize for some inevitable repetition.

In 1884 a Victorian headmaster, Edwin Abbot, wrote the well-known story *Flatland* under the pseudonym of A Square.<sup>1</sup> *Flatland* describes a race of beings who are 2-dimensional; triangles, squares, rectangles, polygons, and circles. They are unaware of the existence of anything else outside their universe. For A Square, it is truly impossible to appreciate the full reality of our 3-dimensional universe, called *Spaceland*. To illustrate this deficiency, Abbot imagines A Square watching a still pond being visited by a 3-dimensional being named A Sphere (Figure 1). A Sphere goes down into the water and rises again before disappearing. A Square can see only the part of the sphere intersecting his plane. He sees only a succession of 2-dimensional circles changing size in time. A Square cannot be convinced that A Sphere is a creature that extends spatially into a third dimension unknown to the Flatlanders. *Flatland* was written 25 years before Einstein's theory of relativity, before the days of space-time when time became the fourth dimension. To continue Abbot's metaphor, Einstein brought us to *Timeland*.

A new frame of thinking in the 20th century has resulted from the discovery in 1944 of nonequilibrium thermodynamics in chemistry by the Nobel Laureate Ilya Prigogine, who coined the paradigm of "self-organization" in chemistry. Self-organization, whereby patterns in space and time emerge from randomness without outside influence, is now known to be the rule rather than the exception in living and nonliving systems made up of many interdependent variables.<sup>2,3</sup> This breakthrough has led to the emergence of a multidimensional universe, to complexity, to *Complexland*.

Complex systems have a number of fundamental characteristics. First and foremost, the interactions between the numerous variables are nonlinear. In linear systems the variables are simply and directly related. Mathematically, a linear relationship can be expressed as a simple equation in which the variables appear

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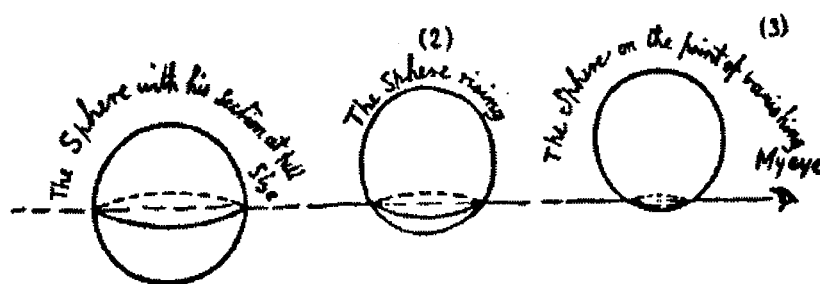
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**Figure 1.** The visitation of A Sphere through Flatland, perceived by A Square as a circle changing in time. (Illustration from *Beyond the Third Dimension: Geometry, Computer Graphics, and Higher Dimension* by Thomas F. Banchoff, © 1990 by Scientific American Library. Reprinted by permission of Henry Holt and Company, LLC.)

only to the power of 1. In a nonlinear system, the many variables in the equations vary with respect to one another by powers of 2 or greater. Nonlinear systems do not obey the simple rules of addition. The whole is more than the sum of its components.

In complex systems there is high sensitivity to initial conditions. A tiny difference in initial conditions can be amplified over time to enormous differences.

Nonlinearity produces feedbacks; the outcome of an effect goes on to trigger more changes, leading to unexpected behaviors. Positive feedbacks amplify the output and tend to undermine the stability of a system. The larger the population, the larger it becomes. Negative feedbacks dampen the output and tend to maintain stability. Predator-prey relationships are regulated by negative feedbacks.

One of the most intriguing aspects of complex systems is that changes do not have to be related to external causes. They are, as already stated, capable of self-organization. Nonlinear interdependent dynamics can create patterns, coherence, networks, copying, synchronization, and synergy.

Complexity theories are probably the broadest of all scientific discoveries of the last century, not only in basic sciences but also in life sciences, where it is now recognized that the main problems of mankind are global and complex. I should like to use my own research to illustrate that computer modeling has begun to explore the behavior of complex systems such as fluid dynamics but that in many of our endeavors we remain to the multidimensional universe of complexity as the Flatlanders were to Spaceland.

### Complexity and Fluid Dynamics

Fluid dynamics studies are still based on nonlinear equations discovered more than 150 years ago, the Navier-Stokes equations. The application of supercomputers to the Navier-Stokes equations has given rise to computational fluid dynamics technology. This marriage has been one of the greatest achievements in fluid dynamics since the equations themselves were formulated. Computer simulation has become an essential tool in such fields as astrophysics, flow machinery, and aircraft design.

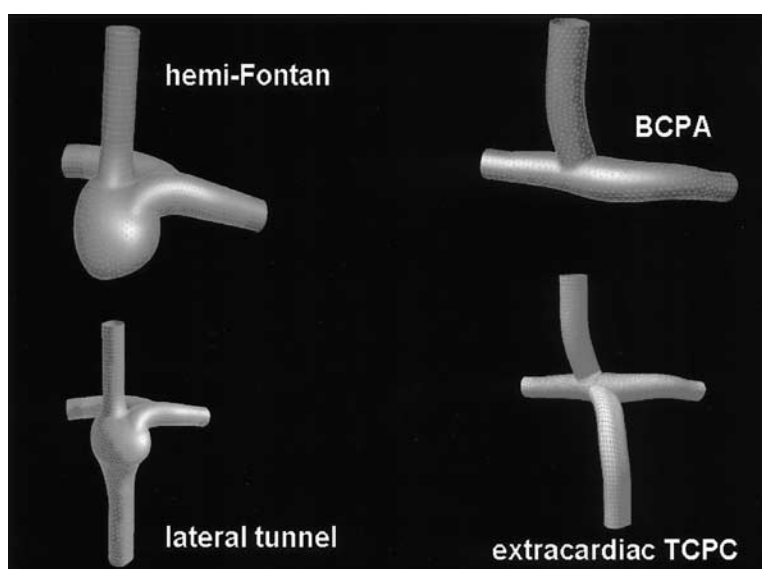
Computational fluid dynamics technology has also been applied to the human cardiovascular system to study, for example, the pathogenesis of atherosclerosis and the formation of aneurysms.<sup>4,5</sup> In collaboration with the School of Bioengineering of Milan, Italy, I have applied computational fluid dynamics to the design and refinement of surgical procedures aimed at mending malformed hearts.

Because the Navier-Stokes equations describe continuous flow fields, and because digital computers are inherently discrete, the equations are necessarily approximated by dividing up space and time into a grid. A 3-dimensional geometric model of the flow domain is divided into a set of simply-shaped regions, called "finite elements." In each element, unknown functions such as pressure and velocity are determined in a number of points or nodes.

We have carried out numerous studies during the past 10 years.<sup>6-8</sup> Recently we collaborated with Ed Bove and colleagues in Ann Arbor, Michigan, to compare the hemi-Fontan circulation with the bidirectional cavopulmonary anastomosis and the lateral tunnel with the extracardiac Fontan circulation (Figure 2).

The 3-dimensional models are linked to unidimensional hydraulic models of the circulation to establish the boundary conditions. Simulations are then undertaken under various inlet and outlet conditions. From these simulations, hemodynamic data such as power dissipation between the cavae and the pulmonary arteries can be calculated (unpublished data). Energy losses are greater for the bidirectional cavopulmonary anastomosis than for the hemi-Fontan circulation and for the extracardiac Fontan circulation than for the lateral tunnel, and these differences increase at higher pulmonary vascular resistance (Table 1).

Since 1950, computer power has increased by a factor of about 10 billion. It doubles roughly every 18 months. Despite such astonishing advances, however, computational fluid dynamics can only handle relatively simple flows with low velocity. Practically, flows that interest scientists most are turbulent ones, those with high Reynolds values. Modeling turbulent flow remains largely beyond the capabilities of today's supercomputers, however, because the time taken



**Figure 2.** Three-dimensional grids of hemi-Fontan circulation combined with bidirectional cavopulmonary anastomosis (BCPA), lateral tunnel, and extracardiac Fontan circulation. TCPC, Total cavopulmonary connection.

**TABLE 1. Hydraulic dissipated power**

Pulmonary arterial resistance (mm Hg/[L · min])	Bidirectional			Extracardiac
	Hemi-Fontan	cavopulmonary anastomosis	Lateral tunnel	total cavopulmonary connection
1	0.88	1.15	3.97	14.75
3	1.70	2.63	6.90	42.89
4	2.11	3.42	8.38	56.63

Hydraulic dissipated power (in milliwatts) is the difference between the total energy at the inlet and at the outlet of the flow domain.

to perform simulations increases as a high power of the velocity. This is because the Navier-Stokes equations, the interactions between the fluid particles, are nonlinear. This leads to multiple effects such as interdependence, in which the flow at one point depends on the flow at many other points, or feedbacks, in which the outcome of an effect goes on to trigger more changes. A combination of positive and negative feedback effects creates the endless swirls, eddies, and vortices of all sizes typical of turbulence. Countless millions of molecules of water seem to know exactly what the others are doing. Turbulence remains one of the greatest challenges of modern science.

### Complexity and Life Sciences

Complexity theories apply to human sciences as well, and I have chosen the analysis of surgical outcomes as an illustration. Medical outcomes result from complex interactions among three sets of complex variables: those related to the patients, those related to the treatments, and those related to

the care providers. If computer modeling in fluid dynamics is still in its infancy, computer simulation in life sciences is at a gestational age.<sup>9</sup>

Statistical methods, however, have become increasingly powerful in the investigation of complex interactions. At this point I should like to acknowledge the enormous contributions of John Kirklin and Eugene Blackstone on outcome analysis and to thank them both for the impact that they have had on my own work.

Most outcome analyses have concentrated mainly on patient-related variables or procedural variables. By and large, human factors related to the care providers have not been included in outcome analyses. Yet investment in human factors is expected to be the most important way to improve safety in high-technology industries such as aviation.

There is no reason to believe that this does not apply to high-technology medicine such as cardiac surgery. It is on these assumptions that we began a research project aiming at incorporating human factors in outcome analyses.<sup>10</sup> This was done in collaboration with Jane Carthey, human factors researcher, James Reason, the father of the organizational accident theory, and Vern Farewell, professor of statistics at University College London.

We took the neonatal arterial switch operation as a model of high-technology surgery. All 243 neonatal arterial switch operations for transposition of the great arteries with or without ventricular septal defect performed by all 21 United Kingdom cardiac surgeons in 16 institutions during an 18-month period were entered into the study. Three sets of data were collected: patient variables, procedural variables, and

**TABLE 2. Major events added to the baseline model**

	Death			Death or near miss		
	Odds ratio	95% Confidence interval	<i>P</i> value	Odds ratio	95% Confidence interval	<i>P</i> value
No. of major events per case	2.4	1.7-3.5	<.001	15	6.0-36	<.001
No. of major events per case +	0.43	0.12-1.5	.19	7.5	2.7-21	<.001
No. of uncompensated major events per case	23	3.4-154	.003	5.3	1.2-23	.026

human factors data. The human factors data were collected by a human factors researcher who attended the operations from induction of anesthesia to admission to the intensive care unit. A detailed description of the operation was written down as the procedure was taking place. This included information on individual and team performance, information on communication with each team and between different teams, and situational and organizational data. From these reports, which I stress were written on-line without knowledge of the outcome to avoid hindsight bias, we extracted errors, or failures, which were categorized as minor or major negative events. Minor events were failures that disrupted the surgical flow of the procedure but in isolation were not expected to have serious consequences for the safety of the patient. Major events, on the other hand, were failures that were likely to have serious consequences for the safety of the patients. Examples of minor and major events are given in Appendix 1.

Major and minor events were judged to be either compensated for or uncompensated. An event was deemed to have been compensated for when the patient recovered or when the consequences of the event were negated by appropriate actions. The clinical outcomes were divided into four categories: (1) extubation within 72 hours with no complications, which occurred in nearly half of the patients; (2) prolonged intubation or reversible morbidity, which occurred in just over a quarter of the patients; (3) survival with near misses, which included major ischemic or hemodynamic problems at the end of the operation, mechanical support with extracorporeal membrane oxygenation (ECMO), severe postoperative arrhythmias, deep-seated infections, and permanent neurologic damage, which occurred in 17.7%; and (4) deaths, which occurred in 6.6% of this population. With grouping of near misses and deaths, the incidence of negative outcomes was about 25%.

The statistical analysis consisted of a multivariate analysis of patient- and procedure-specific variables to generate a baseline logistic regression model for two binary outcomes, the probability of death and the probability of death or near miss. The coronary arterial anatomy was the factor most closely related to both outcomes. Human factors data were then added to the logistic regression model after adjustment for coronary arterial distribution.

For both types of events, minor and major, two analyses were undertaken. The first looked at the total number of negative events for both death and death or near miss outcomes. The second analysis added both the total number of events per case and the number of uncompensated events per case so as to investigate the role of compensation.

Table 2 summarizes the results of adding major events to the baseline model. They have a strong relationship to both outcomes, death and death or near miss, with a *P* value less than .001. Compensated major events, even if multiple, however, did not influence the odds of death, whereas for an uncompensated major event the odds of death increased by a factor of 9 and the odds of death or near miss increased by a factor of 34.

Table 3 depicts the results of adding minor events to the baseline model, and this is an important finding. It shows that both outcomes, death and death or near miss, were also strongly related to the number of minor events per case, with a *P* value of less than .001 for both outcomes. The number of uncompensated minor events per case, however, adds very little to the information provided by the number of minor events. Table 4 shows the results of adding the number of major events, the number of uncompensated major events, and the number of minor events jointly to the baseline model. It shows that even after adjusting for the effects of major and major uncompensated events, there is still suggestive evidence of a link between the number of minor events and death, with strong evidence of a link between the number of minor events and death or near miss.

Because of their immediate potential dramatic consequences, major events are always noticed, and appropriate compensation can prevent their leading to a catastrophe, even if they are multiple. Minor events, on the other hand, are much more insidious. Because of their seemingly benign nature, they are sometimes hardly noticed, and little effort is made to compensate. The main feature of minor events is their multiplicative effect. In isolation they have little impact, but their multiplication has a strong relationship to negative outcomes.

Throughout this research we have established extensive contacts with high-technology industries such as the aviation industry and the car racing industry. One of the most important safety initiatives in aviation has been the intro-

**TABLE 3. Minor events added to the baseline model**

	Death			Death or near miss		
	Odds ratio	95% Confidence interval	P value	Odds ratio	95% Confidence interval	P value
No. of minor events per case	1.5	1.3-1.8	<.001	1.6	1.4-1.9	<.001
No. of minor events per case +	1.1	0.54-2.1	.87	1.2	0.81-1.8	<.37
No. of uncompensated minor events per case	1.5	0.7-3.1	.28	1.4	0.90-2.21	.14

**TABLE 4. Minor and major events analyzed jointly**

	Death			Death or near miss		
	Odds ratio	95% Confidence interval	P value	Odds ratio	95% Confidence interval	P value
No. of major events	0.44	0.12-1.6	.21	6.2	2.0-19	.002
No. of uncompensated major events	13	2.1-83	.006	6.4	0.99-41	.051
No. of minor events	1.4	1.0-2.0	.03	1.4	1.2-1.8	.001

duction of crew resource management training in the 1980s.<sup>11,12</sup> Crew resource management is about error management, which has three lines of defense: prevention, detection, and recovery.

Recent research has shown that the most successful organizations at managing potentially hazardous operations were those that created safety by anticipating and planning for unexpected events and future surprises.<sup>13</sup> There is no need to demonstrate to this audience that anticipation of problems is one of the characteristics of good surgery.

In Formula 1 motor racing, 90% of the outcome of the race depends on the pit stop. Each pit stop is videotaped and observed by human factors experts who score the errors. The highest scores go to the minor errors, those that go undetected by the performers. These are equivalent to the minor events of our study. The health care industry could, in my opinion, benefit greatly from the appointment of human factors observers to help detect errors and consequently improve quality of care.

Error recovery is the third line of defense in error management. It includes tolerance, compensation, and mitigation of adverse events. Errors will never be eradicated, and some are unavoidable. Our study has highlighted the importance of recovery or compensation from major negative events. The racing car industry has made huge investments in recovery, and these have paid off in sharply reduced human casualties, even after the most spectacular crashes. Recovery from major negative events, from serious complications, is known to be one of the hallmarks of the best institutions in healthcare.<sup>14,15</sup> An example of recovery from a major negative event is the rapid deployment of ECMO support after a cardiac arrest in the intensive therapy unit, which has recently contributed to a reduction in mortality in pediatric cardiac surgery.

In the framework of complexity, surgical outcomes could be regarded as the result of synergetic nonlinear interactions between multiple interdependent variables related to patients, procedures, and care providers. As an example I will take again the arterial switch operation and look at the cost of the treatment as an outcome event. In the first scenario, the procedure is completely uneventful. The patient stays in the intensive care unit for 24 hours and returns home within 7 days. The cost is \$40,000 (cost figures in this analysis were kindly provided by Dr Ed Bove, Ann Arbor, Mich). In the second scenario, a rotation of just a few degrees of the left coronary artery during its implantation to the pulmonary artery results in inadequate myocardial perfusion, so that the anastomosis has to be revised, the ventricular function remains poor at the end of the operation, and temporary mechanical support is provided by ECMO for 5 days. The patient spends 3 weeks in the intensive care unit and leaves the hospital in good health after 1 month. The cost is \$94,000. In the third scenario, during ECMO support a kink on the arterial line remains unnoticed for a few minutes because of a faulty alarm system. This results in temporary but profound hypotension from which the patient sustains severe and permanent brain damage requiring lifetime care. The cost of treatment reaches astronomical figures, even without considering the human tragedy.

This is an illustration of nonlinearity, the absence of proportion between input—the arterial switch operation—and output—the cost. A small change in the initial conditions, a few degrees of rotation of the left coronary artery, has a major impact on the outcome. A small event, a faulty alarm system, leads to catastrophic consequences.

This last scenario brings me to address in brief the issues of responsibility and excellence in nonlinear systems. The linear mechanistic view of causality remains the dominant



paradigm of our legal system. In a linear model, the extent of an effect is believed to be similar to the extent of its cause. The punishment can consequently be proportional to the degree of damage effected.<sup>16</sup> Little has changed, I am afraid, since the code of Hammurabi, an extraordinary document set down in black diorite and currently in the Louvre Museum in Paris. This is the first legal document related to medical malpractice and dates from around 2000 bc.<sup>17</sup>

In Law 215 it is stated, "If a doctor has treated a gentleman for a severe wound with a bronze lancet, and has cured the man, he shall receive 10 shekels of silver." This was actually enough to pay a carpenter for 450 working days. In Law 218, which relates to malpractice, one can read, "If a doctor has treated a gentleman for a severe wound with a bronze lancet, and has caused the gentleman to die, one shall cut off his hands." Linear thinking can be dangerous in a nonlinear complex reality, where tiny initial fluctuations may result in a global crisis, where one can become accountable for events that are to some extent uncontrollable.

We see the world of complexity with the eyes of the Flatlander visited by a 3-dimensional sphere, which is perceived as a circle of varying circumferences (Figure 1). We are the slaves of our dimensional prejudices, and we are encouraged to maintain that attitude because of our inability to understand and measure higher dimensions.

This conflict is beautifully illustrated in a wood engraving by Maurits Escher (Figure 3). It shows a 2-dimensional dragon trying very hard to fight his 2-dimensionality by sticking his head and his tail through an open 3-dimensional cube.

We are expected to produce excellence in a world of higher dimensions of which we are fully aware but cannot measure. This is what I would call an epistemologic paradox. Epistemology is the science of knowledge. We know about higher dimensions but we cannot measure them, and this is the paradox.

We are in a situation similar to that of the many sailors who, for hundreds of years, were aware of the existence of longitude but could not measure it until John Harrison designed a clock that kept time at sea.<sup>18</sup> This was the thorniest scientific dilemma of the 18th century. Lacking the ability to measure their longitude, sailors were literally lost at sea as soon as they had lost sight of land. Thousands of lives and fortunes of nations were hanging on a resolution of the longitude problem. In 1714, during the reign of Queen Anne, £20,000 of prize money was offered to anyone who discovered a method or device to measure longitude. Countless proposals were received, some of them from cranks and opportunists, but others were promulgating what we would now call surrogates for the chronometer. Today, we need surrogates to produce excellence in a multidimensional universe that we cannot measure.



**Figure 3. M.C. Escher's "Dragon." From Hofstadter DR. Gödel, Escher, Bach: An Eternal Golden Braid. © 2002 Cordon Art B.V. Baarn, Holland. All rights reserved.**

The way we think about dimensions was shaken in the 1970s by Benoit Mandelbrot, who pointed out that we are surrounded by objects of irregular shapes that have fractions of dimensions.<sup>19</sup> Mandelbrot introduced the concept of fractured dimensionality, and coined the word *fractals* in 1975 to describe those objects. He also discovered that fractals could be generated by computers by means of simple mathematical equations, the output of which is fed back into the same equation as its next input, forming a recursive loop.

Fractal objects are characterized by self-similarity or scale invariance. They are identical across a wide range of scales. Fractal structures are sensitive to initial conditions and the patterns that emerge are unpredictable, but they remain ordered and maintain their compelling beauty. Fractal geometry offers an algorithm to describe the complexity of nature that transects time frame and spatial scale. It is reasonable to suspect that fractal geometry represents a universal language that might apply to human sciences as well.<sup>20</sup> Complex systems such as hospitals, operating



**Figure 4. M.C. Escher's "Smaller and Smaller." From Schattschneider D. M.C. Escher: Visions of Symmetry. © 2002 Cordon Art B.V. Baarn, Holland. All rights reserved.**

rooms, intensive care units, and research laboratories, in which each team, each individual, each element, even at the smallest scales, display the same pattern of symmetry, harmony, and beauty, must have the ingredients of excellence. Each individual, even at the bottom of the ladder, must consequently be made aware of his or her importance and must be accorded the highest respect. Each task, even the ancillary duties, must be given the same attention, the same consideration.

Johann Sebastian Bach's canons, which are among the greatest accomplishments of human intellect, are examples of recursive loops found in fractal geometry.<sup>21</sup> They inspired Maurits Escher in his desire to capture infinity and perfection when he created the magnificent fractal entitled "Smaller and Smaller" (Figure 4).<sup>22</sup>

I suggest that one could usefully apply fractal properties as a surrogate for excellence while waiting for the future generation of supercomputers to generate models of excellence in the complexity of life sciences.

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## Appendix 1: Examples of Minor and Major Events

### Minor Events

- Coordination problem with blood bank or intensive care unit
- Poor preoperative communication (scheduling of cases, fasting)
- Human resource problems (eg, no junior anesthetist)
- Positioning and tension errors by the surgical assistants
- Internal and external distractions
- Equipment breakdowns
- Communication errors between teams
- Absence of a senior team member in the operating room at safety-critical times, inadequate monitoring during transfer to intensive care unit
- Inappropriate task delegation (surgical, anesthetic, perfusion) to inexperienced individuals
- Cognitive tunnel vision

**Major Events**

- Preoperative events such as cardiac perforation during balloon atrial septostomy
- Anesthetic errors, including failure to gain sufficient vascular access, pin-cushioning during insertion of lines leading to a serious cardiac event, and delayed diagnosis of a major deterioration in the patient's condition
- Surgical errors, including laceration of the ductus arteriosus before bypass, serious cannulation problems, aortic tear or massive coronary air embolism during infusion of cardioplegia, damage of coronary artery or of neoaortic valve, and laceration of pulmonary artery
- Major perfusion errors, including pump failure
- Postbypass problems, including delayed diagnosis or misdiagnosis of a serious ischemic event, ventilation errors by the anesthetist, omission of pacing wires in a patient with serious arrhythmias, delayed diagnosis of serious deterioration during transfer to intensive care unit (tamponade), and severe bleeding from poorly secured indwelling catheter (left atrial line)